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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,879	04/09/2007	Augustinus Bader	50326/006001	8676

21559 7590 11/03/2009  
CLARK & ELBING LLP  
101 FEDERAL STREET  
BOSTON, MA 02110

EXAMINER
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DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
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1647

NOTIFICATION DATE	DELIVERY MODE
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11/03/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/583,879	<b>Applicant(s)</b> BADER, AUGUSTINUS	
	<b>Examiner</b> Regina M. DeBerry	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 July 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3,5,6,12,13 and 36-40 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,6,12,13 and 36-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **Status of Application, Amendments and/or Claims**

The amendment and Applicant's arguments, filed 07 July 2009, have been entered in full. Claims 2, 4, 7-11 and 14-35 are canceled. Claims 1, 5, 12, 13 and 36 are amended. New claims 37-40 are added. Claims 1, 3, 5, 6, 12, 13 and 36-40 are under examination.

### **Withdrawn Objections And/Or Rejections**

The rejection to claim 13 under 35 U.S.C. 112, second paragraph, as set forth at page 3 of the previous Office Action (07 January 2007), is *withdrawn* in view of the amendment (07 July 2009).

The rejection to claims 1-3, 11, 13, 19, 20, 22, 31 and 34 under 35 U.S.C. 102(b) as being anticipated by Weiss et al., WO 99/21966, as set forth at pages 4-5 of the previous Office Action (07 January 2007), is *withdrawn* in view of the amendment (07 July 2009).

The rejection to claim 6 under 35 U.S.C. 103(a) as being unpatentable over Weiss et al., WO 99/21966 as applied to claim 1, and further in view of Bhaskaran et al. United States Patent Application Publication US 2004/0136952 A1, as set forth at pages 6-7 of the previous Office Action (07 January 2007), is *withdrawn* in view of the amendment (07 July 2009).

### **Claim Rejections-35 USC § 102(e)**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 5, 12, 13, 36 (and new claims 38 and 39) remain rejected under 35 U.S.C. 102(e) as being anticipated by Brines et al., US 2003/0104988 A1. The basis for this rejection is set forth at pages 5-6 of the previous Office Action (07 January 2007).

Applicant argues that Brines et al. does not teach the use of EPO or any other compound for promoting structural regeneration of the liver after surgical liver resection and/or the use of EPO in combination with a skin graft to heal burn wounds.

Applicant's arguments have been have been fully considered but are not deemed persuasive. The Brines et al. reference meets the limitations of the amended and new claims. Brines et al. teach methods and compositions for protecting or enhancing EPO-responsive cells, tissues, organs, or body part function or viability *in vivo*, *in situ*, *ex vivo* in mammals by systemic or local administration of EPO and derivatives thereof, including EPO-receptor binding domain molecules (abstract; paras 0008 and 0030)(**applies to claim 3 and 38**). Brines et al. teach that EPO responsive cells, tissue, organs include **skin and liver**. Brines et al. teach the preservation of cells, tissues, or organs for either auto-transplant or xeno-transplant (para 0025). The cells, tissues, organs are isolated from a mammal, such as those intended for transplant. Brines et al. teach that cells, tissues or organs may be bathed in a solution comprising EPO prior to transplant, surgery, etc in order to protect said cells, tissues or organs (paras 0005,

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0024-0026, 0028 0054, 0056 and 0127)(**applies to claim 36**). Brines et al. teach EPO can be administered to prevent injury or tissue damage during surgical procedures such as **tumor resection** (paras 0098 and 0127), **burn injuries** (para 14)(**applies to claims 1 and 36**). Brines et al. teach the regeneration of tissue or organ by exposure to EPO (para 0050). Brines et al. teach various modes of EPO administration including systemic and topical administration (paras 0029, 0114, 0125 and 0139)(**applies to claims 12 and 13**). Brines et al. teach that it may desirable to administer EPO locally to the area in need of treatment during surgery or topical administration in conjunction with wound dressing, injection, local infusion, implants (para 0126). Brines et al. teach the use of glycosylated variants of EPO. Brines et al. teach that EPO muteins have additional number of glycosylation sites (para 0064)(**applies to claims 5 and 39**).

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

### **Claim Rejections - 35 USC § 103(a)**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 6 (and new claim 40) remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Brines et al., US 2003/0104988 A1 as applied to claims 1 and 36

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above, and further in view of Bhaskaran et al. United States Patent Application Publication US 2004/0136952 A1. The basis for this rejection is set forth at pages 7-8 of the previous Office Action (07 January 2007).

Applicant argues that Bhaskaran does not remedy the deficiencies of Brines et al., as it fails to teach or suggest a method for promoting structure tissue regeneration of the liver after surgical liver resection in an individual having a benign or malignant liver tumor.

Applicant's arguments have been fully considered but are not found persuasive. The teachings of Brines et al. are described above. Brines et al. do not teach attaching EPO to polyethylene glycol (PEG). Bhaskaran et al. teach the conjugation between PEG and various proteins (abstract; paragraph 0003). Bhaskaran et al. teach that the attachment of PEG to proteins have been shown to stabilize the protein, improve the bioavailability and/or reduce the immunogenicity *in vivo* (paragraphs 0007, 0017-0019). Proteins that can be conjugated to PEG include EPO (paragraph 0021 and claims). Bhaskaran et al. teach that the coupling of the polymer near one or more glycosylation sites mimics the beneficial effects of glycosylation of the protein (paragraphs 0023, 0095, 0099).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of regenerating EPO-responsive mammalian cells and their associated cells, tissues and organs by administering EPO as taught by Brines et al., by employing an EPO conjugated with PEG as taught by Bhaskaran et al. with a reasonable expectation of success. The motivation and expected success is

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provided by Brines and Bhaskaran. Brines et al. teach methods of regenerating cells, tissues and organs by administering EPO. Bhaskaran et al. teach that the attachment of PEG to proteins have been shown to stabilize the protein, improve the bioavailability and/or reduce the immunogenicity *in vivo*. It would be obvious to one of skill in the art to want to utilize an EPO that has a long half-life and low immunogenicity.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

## **NEW REJECTIONS/OBJECTIONS**

### **Claim Rejections-35 USC § 112, First Paragraph, Written Description (New Matter)**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed:

"..of burn wounds in an individual using a skin graft without the occurrence of scarring, the method comprising topically administering to said individual EPO, EMP, or NESP" (claim 36).

"..EPO, EMP or NESP is administered after surgical resection in an amount of 100-150 IU/kg of" (claim 37).

Applicant's amendment, filed 07 July 2007, asserts that no new matter has been added and directs support to paragraph 0185 (for claim 36) and paragraph 0158 (for claim 37) of the published application for support for the written description for the above-mentioned "limitations".

The Examiner has found the following teaching: In 8 burned patients, the donor site of the skin graft healed 50% more quickly on administration of EPO. **Two second-degree (grade 2B) burn wounds in the face healed without scarring if EPO was given to the patient.** Without administration of EPO, wounds of this type healed with scarring (see para 0185).

The wording or connotation of instant claim 36 is not readily apparent from said section.

Lastly, the Examiner has found support for 100-150 IU/kg of Epoietin alpha (see paras 0149, 0151, 0155, 0158 and 0159) and support for 10,000 or 40,000 IU of EPO (see paras 0152, 0165 and 0179). The Examiner has not found support for 100-150 IU/kg of EPO, EMP or NESP.

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations". The specification does not provide direction for



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the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide specific written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

#### **Claim Rejections-35 USC § 112, Second Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim is indefinite because of the limitation, "...without the occurrence of scarring..". It is unclear if the instant claim encompasses an activity directed to scarring (i.e. treating, healing, preventing and/or inhibiting scarring). The metes and bounds of the claim cannot be determined.

### **Conclusion**

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/  
Primary Examiner, Art Unit 1647

/R. M. D./  
Examiner, Art Unit 1647  
10/26/09